Complete Summary

GUIDELINE TITLE

Practice guidelines for the management of patients with blastomycosis.

BIBLIOGRAPHIC SOURCE(S)

Chapman SW, Bradsher RW, Campbell GD, Pappas PG, Kauffman CA. Practice guidelines for the management of patients with blastomycosis. Infectious Diseases Society of America. Clin Infect Dis 2000 Apr;30(4):679-83. [21 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Blastomycosis (disease caused by the fungus Blastomyces dermatitidis)

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Infectious Diseases
Internal Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide recommendations for the optimal treatment of the pulmonary and extrapulmonary forms of blastomycosis

TARGET POPULATION

Patients with blastomycosis

INTERVENTIONS AND PRACTICES CONSIDERED

Antifungal Therapy

- Amphotericin B
- Lipid preparations of amphotericin B
- Ketoconazole
- Itraconazole
- Fluconazole

MAJOR OUTCOMES CONSIDERED

- Abatement of symptoms and signs of blastomycosis
- Eradication of Blastomyces dermatitidis from involved tissue
- Drug toxicity
- Relapse rates

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Grades reflecting the quality of evidence on which recommendations are based:

I. Evidence from at least one properly randomized, controlled trial

II. Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from more than one center), from multiple time-series studies, or from dramatic results of uncontrolled experiments
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not applicable

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

These guidelines are the consensus opinion of an expert panel representing the National Institute of Allergy and Infectious Diseases Mycoses Study Group and the Infectious Diseases Society of America.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of recommendation:

A. Good evidence to support a recommendation for use
B. Moderate evidence to support a recommendation for use
C. Poor evidence to support a recommendation
D. Moderate evidence to support a recommendation against use
E. Good evidence to support a recommendation against use

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Excerpted by the National Guideline Clearinghouse (NGC)

Each recommendation includes a ranking for the strength and the quality of evidence supporting it. Definitions of the levels of evidence (I-III) and grades of recommendation (A-E) are repeated at the end of the Major Recommendations field.

Pulmonary Blastomycosis

All immunocompromised patients and patients with progressive pulmonary infection should be treated. Spontaneous cure has been well documented for patients with acute pulmonary infection. Thus, in selected cases, patients may be closely monitored for resolution or progression of disease. Complicating this management decision, some patients present with serious extrapulmonary disease after the resolution of pulmonary infection. Patients must therefore be carefully evaluated for extrapulmonary disease before a decision is made to withhold therapy.

Patients with life-threatening disease, such as acute respiratory distress syndrome, should be treated with amphotericin B (0.7–1 mg/kg/day; total dose, 1.5–2.5 grams; see Table 1 of the original guideline document) (AII). Therapy for some patients may be switched to itraconazole (200–400 mg/day) after clinical stabilization with an initial course of amphotericin B treatment, usually a minimum dose of 500 mg (BIII).

Patients with mild to moderate disease should be treated with itraconazole at a dosage of 200–400 mg/day for a minimum of 6 months (AII). An alternative to itraconazole includes 6 months of either ketoconazole at a dosage of 400–800 mg/day (BII) or fluconazole at a dosage of 400–800 mg/day (BII). For patients who are unable to tolerate an azole or whose diseases progress during azole treatment, therapy should be changed to amphotericin B (0.5–0.7 mg/kg/day; total dose, 1.5–2.5 grams) (AII).

Disseminated Blastomycosis, Extrapulmonary

All patients with disseminated disease require treatment. The presence or absence of central nervous system infection is the critical factor for determining therapy.

Patients with central nervous system infection should receive a dosage of amphotericin B of 0.7–1 mg/kg/day (total dose, at least 2 grams) (AII). The use of lipid formulations of amphotericin B has not been reported for central nervous system blastomycosis, but this treatment may be an alternative for patients unable to tolerate amphotericin B because of toxicity. Azoles should not be considered for primary treatment of patients with central nervous system blastomycosis (EIII). However, fluconazole, because of its excellent cerebral spinal fluid penetration, could possibly be a consideration at higher dosages (minimum, 800 mg/day) in special circumstances (CIII).

Patients with life-threatening disseminated disease should be treated with amphotericin B (0.7–1 mg/kg/day; total dose, 1.5–2.5 grams) (AII). Therapy for some patients may be switched to itraconazole after clinical stabilization with amphotericin B (BIII). Patients with mild to moderate disseminated blastomycosis that does not involve the central nervous system (CNS) should be treated with itraconazole (200–400 mg/day) for at least 6 months (AII). Ketoconazole and fluconazole, both at dosages of 400–800 mg/day, are alternatives to itraconazole (BII). Bone disease is more difficult to treat and more likely to relapse. Therefore, patients with blastomycotic osteomyelitis should receive at least 1 year of treatment with an azole (BIII). For patients whose diseases progress during treatment with an azole or who are unable to tolerate an azole because of toxicity, amphotericin B (0.5–0.7 mg/kg/day; total dose, 1.5–2.5 grams) is recommended (AII).

Blastomycosis in the Immunocompromised Host

Recent reports indicate that Blastomyces dermatitidis may infrequently act as an opportunistic pathogen, notably in patients who are in the late stages of acquired immune deficiency syndrome (AIDS), transplant recipients, and patients treated with immunosuppressive or cytotoxic chemotherapy. Disease in these patients is more aggressive and more often fatal than disease in the normal host. Pulmonary disease is more likely to present with diffuse pulmonary infiltrates and respiratory failure. Dissemination to multiple organs, including the central nervous system, also occurs more frequently. Mortality rates of 30%–40% have been reported, and most deaths attributed to blastomycosis occur during the first few weeks of therapy. Thus, early and aggressive treatment with amphotericin B (0.7–1 mg/kg/day) is indicated for blastomycosis in the immunocompromised patient (AII). Most experts recommend a total dose of 1.5–2.5 grams, although treatment for selected patients without central nervous system infection may be switched to itraconazole after clinical stabilization with amphotericin B (usually a minimum dose of 1 gram) (BIII).

Despite amphotericin B treatment, frequent relapses occur in patients with AIDS and in those patients who continue immunosuppressive therapy. Some authorities therefore recommend chronic suppressive therapy with an azole, preferably itraconazole, for those patients who respond to a primary course of amphotericin B treatment (BIII). Treatment with ketoconazole is discouraged because relapse rates are higher (DIII). Fluconazole treatment may be given special consideration for selected patients who have had central nervous system disease or patients unable to tolerate itraconazole owing to toxicity or drug interactions (BIII).

Special Circumstances

Pregnancy

Amphotericin B is the drug of choice for treating blastomycosis in pregnant women (AII). The azoles should never be used as treatment for this patient cohort because of their embryotoxic and teratogenic potential (EIII).

Pediatrics

Although blastomycosis is less commonly described in children, the clinical spectrum of disease is similar to that described in adults. However, a recent report has indicated that the diagnosis of blastomycosis in children, compared with adults, is more difficult to establish and that the response to oral azoles in children is less than satisfactory. Children with life-threatening or central nervous system disease should be treated with amphotericin B (AII). Itraconazole, at a dosage of 5–7 mg/kg/day, has been used successfully as treatment of a limited number of pediatric patients with non–life-threatening non-central nervous system disease (BIII).

Definitions of Strength of Recommendation and Quality of Evidence Ratings:

Quality of evidence:

I. Evidence from at least one properly randomized, controlled trial
II. Evidence from at least one well-designed clinical trial without randomization, from cohort or case-control analytic studies (preferably from more than one center), from multiple time-series studies, or from dramatic results of uncontrolled experiments
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

Strength of recommendation:

A. Good evidence to support a recommendation for use
B. Moderate evidence to support a recommendation for use
C. Poor evidence to support a recommendation
D. Moderate evidence to support a recommendation against use
E. Good evidence to support a recommendation against use

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Before antifungal therapy became available, blastomycosis was thought to have a chronic progressive course with eventual dissemination and associated mortality rates of up to 90%. Conversely, the recent studies, which were reviewed in the

guideline, have reported cure rates of >85% and mortality rates of <10% in conjunction with the appropriate treatment of blastomycosis.

Subgroups Most Likely to Benefit:

Immunocompromised patients and patients with progressive pulmonary disease or extrapulmonary disease.

POTENTIAL HARMS

Antifungal Therapy

- Conventional amphotericin B is associated with significant toxicity, including infusion-related events, such as chills, fever, headache, nausea and vomiting, and dose-limiting nephrotoxicity.
- Lipid formulations of amphotericin B, although offering several therapeutic advantages over conventional amphotericin B, are considerably more expensive, ranging from 10- to 20-fold higher in cost.
- One potential limitation of the azole antifungal drugs is the frequency of their interactions with coadministered drugs, which results in adverse clinical consequences. One type of azole-drug interaction may lead to decreased plasma concentration of the azole, related to either decreased absorption or increased metabolism of the azole. A second type of azole-drug interaction may lead to an unexpected toxicity of the coadministered drug, relating to the ability of the azoles to increase plasma concentrations of other drugs by altering hepatic metabolism via the cytochrome P-450 system.
- A second potential limitation of the azoles is the emergence of resistance of fungal organisms, especially Candida species, to fluconazole.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Safety
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Chapman SW, Bradsher RW, Campbell GD, Pappas PG, Kauffman CA. Practice guidelines for the management of patients with blastomycosis. Infectious Diseases Society of America. Clin Infect Dis 2000 Apr;30(4):679-83. [21 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Apr

GUIDELINE DEVELOPER(S)

Infectious Diseases Society of America - Medical Specialty Society

SOURCE(S) OF FUNDING

Infectious Diseases Society of America (IDSA)

GUIDELINE COMMITTEE

Infectious Diseases Society of America (IDSA) Practice Guidelines Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors: Stanley W. Chapman, Robert W. Bradsher, Jr., G. Douglas Campbell, Jr., Peter G. Pappas, and Carol A. Kauffman.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Infectious Diseases Society of America (IDSA) Web site. Also available in HTML format.

Print copies: Available from the University of Chicago Press; fax: (773) 702-6096.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Kish MA. Guide to development of practice guidelines. Clinical Infectious Diseases 2001;32:851-4.
- Gross PA. Practice guidelines for infectious diseases: Rationale for a work in progress. Clin Infect Dis. 1998 May;26(5):1037-41.
- Gross PA, Barrett TL, Dellinger EP, Krause PJ, Martone WJ, McGowan JE Jr, Sweet RL, Wenzel RP. Purpose of quality standards for infectious diseases. Infectious Diseases Society of America. Clin Infect Dis 1994 Mar;18(3):421.

Electronic copies: Available from the Infectious Diseases Society of American (IDSA) Web site.

Print copies: Available from Infectious Diseases Society of America, 66 Canal Center Plaza, Suite 600, Alexandria, VA 22314.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on May 1, 2001. The information was verified by the guideline developer as of June 29, 2001.

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